

THAT WHICH IS CLAIMED:

1. A method for identifying genes and their expression products as screening targets for drugs for treating addictive disorders, the method comprising:
 - 5 (a) determining the expression level of one or more genes in a first sample from one or more subjects affected by an addictive disorder;
 - (b) determining the expression level of said one or more genes in a second sample from one or more control subjects;
 - (c) for each of said one or more genes, comparing the expression
10 level measured in step (a) with the expression level measured in step (b);wherein a gene whose expression level is significantly increased or significantly decreased in said one or more subjects affected by an addictive disorder in comparison with the expression level in said one or more control subjects is identified, along with its expression products, as a screening target for drugs for
15 treating addictive disorders.
2. The method of claim 1, wherein said first sample and said second sample comprise cells that are affected by addictive disorders.
- 20 3. The method of claim 2, wherein said cells that are affected by addictive disorders are selected from the group consisting of ventral tegmental area cells and lateral substantia nigra cells.
4. The method of claim 1 wherein said addictive disorder is cocaine
25 addiction.
5. The method of claim 1, wherein said first sample and said second sample comprise cells from human post-mortem tissues.
- 30 6. A method for producing an expression profile comprising values representing the expression levels of genes whose expression is associated with addictive disorders, the method comprising:

- (a) determining the expression level of one or more genes in a first sample from one or more subjects affected by an addictive disorder;
- (b) determining the expression level of said one or more genes in a second sample from one or more control subjects;
- 5 (c) identifying genes whose expression level is significantly increased or significantly decreased in said one or more subjects affected by drug addiction in comparison with the expression level in said one or more control subjects; and
- (d) producing an expression profile comprising values representing
10 the expression levels of genes of genes identified in step (d) in subjects affected by an addictive disorder.

7. The method of claim 6, wherein said one or more genes are selected from the group consisting of the genes shown in Tables 3, 4, and 5.

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8. The method of claim 6, wherein said expression profile comprises values representing the expression levels of at least five genes

9. The method of claim 6, wherein said expression profile comprises
20 values representing the expression levels of at least ten genes

10. The method of claim 6, wherein said expression profile comprises values representing the expression levels of at least ten genes selected from the group consisting of the genes shown in Tables 3, 4, and 5.

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11. The method of claim 6, wherein said expression profile comprises values representing the expression levels of genes selected from the genes shown in Table 3.

30 12. The method of claim 6, wherein said first sample and said second sample comprise cells selected from the group consisting of ventral tegmental area cells and lateral substantia nigra cells.

13. The method of claim 12, wherein said first sample and said second sample comprise at least 50% of a cell type selected from the group consisting of ventral tegmental area cells and lateral substantia nigra cells.

5 14. The method of claim 6 wherein said addictive disorder is cocaine addiction.

15 15. The method of claim 6 wherein said first sample and said second sample comprise cells from human post-mortem tissues.

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16. A method for predicting whether a compound will be addictive in humans, said method comprising:

(a) providing a reference expression profile associated with an addictive disorder, wherein said expression profile comprises values representing the expression level of one or more genes whose expression is associated with an addictive disorder in one or more samples from one or more subjects affected by the addictive disorder;

(b) providing a test expression profile comprising values representing the expression level of said one or more genes in a sample comprising cells that been contacted with the compound; and

(c) determining whether said test expression profile shares sufficient similarity to said reference profile;

wherein a determination that the test expression profile shares sufficient similarity to the reference profile results in a prediction that the compound will be addictive in humans.

17. The method of claim 16, wherein said reference expression profile is produced according to the methods of claim 6.

30 18. The method of claim 16, wherein said reference expression profile is produced according to the methods of claim 7.

19. The method of claim 16, wherein said reference expression profile comprises values representing the expression levels of at least five genes selected from the group consisting of the genes shown in Tables 3, 4, and 5.

5 20. The method of claim 16, wherein said reference expression profile comprises values representing the expression levels of genes selected from the genes shown in Table 3.

21. In a method of screening for therapeutic compounds for use in treating
10 addictive disorders, an improvement comprising the use of a target identified by the method of any one of claims 1-4.

22. The method of claim 21, where wherein said addictive disorder is cocaine addiction.

15 23. A method of screening for therapeutic compounds for use in treating addictive disorders comprising screening for modulators of a target gene selected from the group consisting of the genes listed in Table 3, the genes listed in Table 4, the genes listed in Table 5, and the expression products of said genes.

20 24. A method of screening for therapeutic compounds for use in treating addictive disorders comprising screening for inhibitors of a target gene selected from the group consisting of the genes listed in Table 5 and the expression products of said genes.

25 25. A method of screening for therapeutic compounds for use in treating addictive disorders comprising screening for activators of a target gene selected from the group consisting of the genes listed in Table 4 and the expression products of said genes.

30 26. A method for evaluating a candidate drug to determine whether it will have therapeutic efficacy in treating an addictive disorder, the method comprising:

- (a) determining the expression level of one or more genes in a first sample from a subject affected by an addictive disorder prior to treatment with the candidate drug, wherein expression of said one or more genes is associated with the addictive disorder;
- 5 (b) determining the expression level of said one or more genes in a second sample from the subject following treatment with the candidate drug;
- (c) for each of said one or more genes, comparing the expression level measured in step (a) with the expression level measured in step (b) to determine the change in the expression level of said genes following treatment with the
- 10 candidate drug.

27. The method of claim 26, wherein said one or more genes comprise at least five genes selected from the group consisting of genes shown in Tables 3, 4, and 5.

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28. The method of claim 26, wherein said one or more genes are selected from the genes shown in Table 3.

29. The method of claim 26, where wherein said addictive disorder is cocaine addiction.

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30. An array comprising a substrate having a plurality of addresses, wherein each address has disposed thereon a capture probe that can specifically bind a nucleic acid molecule that is differentially expressed in subjects affected by cocaine addiction.

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31. The array of claim 30, wherein the nucleic acid molecule that is differentially expressed in subjects affected by cocaine addiction is selected from the group consisting of the genes shown in Tables 3, 4, and 5.

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32. The array of claim 31, wherein the substrate has greater than 10 addresses.

33. The array of claim 32, wherein the substrate has greater than 20 addresses.
34. The array of claim 33, wherein the substrate has greater than 50 addresses.
35. The array of claim 34, wherein the substrate has greater than 100 addresses.
36. The array of claim 31, wherein the substrate has no more than 500 addresses.
37. A kit for predicting whether a compound will be addictive in humans, the kit comprising
- (a) an array comprising a substrate having a plurality of addresses, wherein each address has disposed thereon a capture probe that can specifically bind a nucleic acid molecule that is differentially expressed in subjects affected by an addictive disorder; and
- (b) a computer-readable medium having a digitally-encoded expression profiles having values representing the expression of a nucleic acid molecules detected by the array.
38. The kit of claim 37, wherein said array is the array of claim 31.
39. A computer-readable medium having a digitally-encoded expression profile comprising one or more values representing the expression levels of a gene that is differentially expressed in cocaine overdose victims.
40. The computer readable medium of claim 39, wherein the expression profiles comprise values selected from the group consisting of values representing the expression levels of the genes shown in Tables 3, 4, and 5.

41. The computer readable medium of claim 40, wherein the expression profiles comprise values selected from values representing the expression levels of at least 10 genes selected from the genes show in Tables 3, 4, and 5.

5 42. The computer readable medium of claim 41, wherein the expression profiles comprise values selected from values representing the expression levels of at least 20 genes selected from the genes show in Tables 3, 4, and 5.

43. The computer readable medium of claim 42, wherein the expression
10 profiles comprise values selected from values representing the expression levels of at least 50 genes selected from the genes show in Tables 3, 4, and 5.

44. The computer readable medium of claim 43, wherein the expression
15 profiles comprise values selected from values representing the expression levels of at least 100 genes selected from the genes show in Tables 3, 4, and 5.

45. A kit use in a method of evaluating the therapeutic efficacy of a candidate drug in treating an addictive disorder, the kit comprising

(a) an array comprising a substrate having a plurality of addresses,
20 wherein each address has disposed thereon a capture probe that can specifically bind a nucleic acid molecule that is differentially expressed in subjects affected by an addictive disorder; and

(b) a computer-readable medium having a digitally-encoded
expression profiles having values representing the expression of a nucleic acid
25 molecules detected by the array.

46. The kit of claim 45, wherein said array is the array of claim 31.

47. The method of claim 1, wherein said first sample and said second
30 sample comprise cells from a rodent model for cocaine addiction.

48. The method of claim 6, wherein said one or more genes are selected from the group consisting of the genes shown in Table 3, 4, 5, and 6.

49. The method of claim 16, wherein said reference expression profile comprises values representing the expression levels of at least five genes selected from the group consisting of the genes shown in Tables 3, 4, 5, and 6.

50. A method of screening for therapeutic compounds for use in treating addictive disorders comprising screening for modulators of a target gene selected from the group consisting of the genes listed in Table 6, and the expression products of said genes.

51. The method of claim 26, wherein said one or more genes comprise at least five genes selected from the group consisting of genes shown in Tables 3, 4, 5, and 6.

52. The array of claim 30, wherein the nucleic acid molecule that is differentially expressed in subjects affected by cocaine addiction is selected from the group consisting of the genes shown in Tables 3, 4, 5, and 6.

53. The computer readable medium of claim 39, wherein the expression profiles comprise values selected from the group consisting of values representing the expression levels of the genes shown in Tables 3, 4, 5, and 6.